UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,134	09/14/2006	Irina Velikyan	PH0334	7198

36335 7590 06/06/2008
GE HEALTHCARE, INC.
IP DEPARTMENT
101 CARNEGIE CENTER
PRINCETON, NJ 08540-6231

EXAMINER	
PERREIRA, MELISSA JEAN	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
06/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,134	VELIKYAN ET AL.	
	Examiner	Art Unit	
	MELISSA PERREIRA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/20/08 has been entered.

Previous Claims and Rejections Status

2. The rejection of claims 1-15 under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (WO03/059397) in view of the combined disclosures of Yngve (Int. Diss. Abs. **2001**, 62) and Bottcher et al. (US 5,439,863) and in further view of Maier-Borst et al. (GB 2056471A) is maintained.

3. The provisional rejections of claims 1,3-7 and 15 under 35 U.S.C. 101 as claiming the same invention as that of claims 8-14 of copending Application No. 10/552,206 and of claims 1,3-6 and 9-14 under 35 U.S.C. 101 as claiming the same invention as that of claims 1-4,8-13 of copending Application No. 11/358,681 are maintained.

4. The provisional rejections of claims 1-15 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1,2,8-15,18, and 19 of copending Application No.10/552,206 and of claims 1-14 on the ground of

nonstatutory obviousness-type double patenting as being unpatentable over claims1-5 and 8-14 of copending Application No. 11/358,681 are maintained.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (WO03/059397) in view of the combined disclosures of Yngve (Int. Diss. Abs. **2001**, 62) and Bottcher et al. (US 5,439,863) and in further view of Maier-Borst et al. (GB 2056471A).

7. Griffiths et al. (WO03/059397) discloses a radiolabeling method for the preparation of a NOTA or DOTA (containing N hard donor atoms) labeled ^{68}Ga for use in PET (p18, paragraph 1) and the development of a ^{68}Ge/^{68}Ga in-house titanium dioxide generator (p7, paragraph 3; p8). The macrocyclic-chelating agent, such as DOTA may be linked to a peptide that can target the site of a disease, thus generating a bifunctional chelating agent comprising a targeting vector which will be site-specific (p9, paragraph 1). The method of producing a radiolabeled gallium complex involves reacting the solution of a peptide labeled macrocyclic chelate with the ^{68}Ga diluted from the ^{68}Ge/^{68}Ga titanium dioxide generator which can be fitted with an anion-exchange membrane, such as a Q5F cartridge (p12, paragraph 1; p13, paragraph 2; p16,

paragraph 2). Griffiths et al. (WO03/059397) does not disclose the synthesis of the ^{68}Ga-DOTA-peptide complex via microwave, a ^{68}Ga-DOTA-oligonucleotide or the anion exchanger of the instant claims.

8. Yngve (Int. Diss. Abs. **2001**, *62*) discloses the preparation of a phosphorothiolated ^{68}Ga-DOTA-oligonucleotide and a ^{68}Ga-DOTA-octreotide for use in PET (p12, paragraph 1; p21, last paragraph; p40, paragraph 2). The production of ^{68}Ga is from a generator system via an ion-exchange column (p39, paragraph 3). The labeling of octreotide (a synthetic octapeptide that show high selectivity for the somatostatin receptor) has been widely investigated due to the role of somatostatin for tumour diagnosis and treatment. Radiolabeled octreotides are routinely used for clinical applications.

9. Bottcher et al. (US 5,439,863) discloses the preparation of metal complex salts via microwave irradiation (column 3, line 45). The complexes are prepared from metal ions, such as those of the second and third main group, not excluding gallium and multitoothed chelating ligands that occupy more than one coordination site on the central metal atom (column 3, lines 55-59; column 4, lines 44-46). The ligands of the disclosure may include those with dioxime (N and O containing), etc. groups (column 5, lines 20-24). The use of microwave as the high-energy input allows for a continuous conversion, single-stage reaction with short reaction time and ease of separation of the formed complexes (column 4, line 19; column 5, lines 66+; column 6, lines 1-5).

10. Maier-Borst et al. (GB 2056471A) discloses the separation of ^{68}Ga for its parent nuclide with water via passing the eluant from a generator column into an anion

exchanger comprising quaternary ammonium groups incorporated in a matrix of styrene and divinylbenzene and washing the anion exchanger with water (p4, lines 44-48).

11. At the time of the invention it would have been obvious to produce a ^{68}Ga-DOTA-oligonucleotide complex (see disclosures above) for use as a PET tracer via the production of ^{68}Ga from a ^{68}Ge/^{68}Ga titanium dioxide generator as disclosed by Griffiths et al. The microwave synthesis technique for the method of producing metal-chelate complexes was known by Bottcher et al. thus, it would have been obvious to utilize the microwave acceleration technique for a faster, more reproducible preparation of the ^{68}Ga-DOTA-oligonucleotide complex, such as that of Yngve to generate a complex useful in the treatment or diagnosis of tumours with minimal side product formation. Microwave acceleration techniques have been utilized since the 1980's in a number of production methods for radioactive precursors and radiotracers labeled with positron-emitting nuclides. The microwave method is mostly associated with shortened reaction times and encompasses the microwave conditions of the instant claims. Since the microwave technique was known in the art (Bottcher et al.) one would have a reasonable expectation of success for preparing radiotracer via labeling reactions with this improved microwave technique. The disclosures of Griffiths et al. and Bottcher et al. are both drawn to the same utility (i.e. the preparation of metal complexes) and therefore the results would be predictable for a faster and more efficient preparation via microwave.

12. It would have been obvious to utilize an anion exchanger of Maier-Borst et al. to separate ^{68}Ga from its parent nuclide since no chelating agent is required for

separation. It is known in the art to add a chelating agent, such as EDTA to elute ^{68}Ga from an aluminum oxide exchanger. The disadvantage of forming the ^{68}Ga-EDTA complex is that the complex has to be destroyed before further processing to obtain radiopharmaceutical agents which is time-consuming and expensive (see Maier-Borst et al. p1, lines 10-16).

Response to Arguments

13. Applicant's arguments filed 2/20/08 have been fully considered but they are not persuasive.

14. Applicant asserts that Griffiths et al. does not disclose the preparation of the agents via microwave acceleration.

15. The reference of Griffiths et al. was not used to teach of the preparation of the agents via microwave acceleration but to provide for the ^{68}Ga radiolabeled NOTA or DOTA and their use in PET. The ^{68}Ga- DOTA may be further linked to a peptide for targeting a specific cell, organ, tumor, etc. Griffiths et al. was also used to teach of the purification of ^{68}Ge/^{68}Ga via in-house titanium dioxide generator which can be fitted with an anion-exchange membrane.

16. Applicant asserts that Yngve did not use microwave heating to carry out the coordination chemistry (complexation of gallium by chelates).

17. The reference of Yngve was not used to teach of microwave heating to carry out the coordination chemistry (complexation of gallium by chelates) but to teach of the preparation of a phosphorothiolated ^{68}Ga-DOTA-oligonucleotide and a ^{68}Ga-DOTA-

octreotide for use in PET. In combination with Griffiths et al., it would be obvious to substitute the oligonucleotide of Yngve for the peptide of Griffiths et al. as both DOTA complexes are used for PET.

18. Applicant asserts that Bottcher et al. concerns inorganic chemistry of salts and not coordination chemistry of the instant invention.

19. Bottcher et al. teaches of neutral transition metal complexes salts where the metal complex salt/transition complex is coordinated to a ligand, where the ligand is coordinated around a central atom (column 1, lines 16-17; column 2, lines 25-29). The transition complexes encompass the coordination complexes of the instant claims. The production of neutral metal complex salts is in substantially quantitative yield and high purity via microwave (column 2, lines 30-33; column 3, lines 45 and 55-59).

20. Applicant asserts that the reference of Maier-Borst et al. is aimed to synthesize an anion exchange resin for the separation of gallium-68 from germanium-68 thus avoiding the use of EDTA for elution as it was done before the 1980's.

21. The instant claims are drawn to the method of obtaining ^{68}Ga from a ^{68}Ge/^{68}Ga generator with an anion exchanger, such as polystyrene-divinylbenzene and a dilute HCl solution. The method of Maier-Borst et al. is drawn to obtaining ^{68}Ga from a ^{68}Ge/^{68}Ga generator with an anion exchanger, such as styrene and divinylbenzene and a dilute HCl solution (p1, lines 59-63) and therefore the method of Maier-Borst et al. encompasses the method of the instant claims. The instant claims do not provide the limitations of a preconcentration procedure.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reac

hed on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/
Examiner, Art Unit 1618